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| 09/886,208 | 06/22/2001 | Steven F. Fabijanski | S&B-C099 | 5580 |

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GEORGE A. LOUD
3137 MOUNT VERNON AVENUE
ALEXANDRIA, VA 22305

| EXAMINER | |
|---|---|
| FOX, DAVID T | |

| ART UNIT | PAPER NUMBER |
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| 1638 | |

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/886,208 | Fabijanski et al |
| **Examiner** | **Group Art Unit** |
| FOX | 1638 |

*—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

☑ Responsive to communication(s) filed on 11/4/02.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

**Disposition of Claims**

☑ Claim(s) 98 - 119 is/are pending in the application.

Of the above claim(s) 100, 102, 107-108, 114-119 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 98, 99, 101, 103-106, 109-113 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☑ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Pri rity under 35 U.S.C. § 119 (a)-(d)**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

**Attachment(s)**

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

**Office Action Summary**

Applicant's election with traverse of Group I in Paper No.11 is acknowledged. The traversal is on the ground(s) that the inventions all depend upon claim 98 and so are related, and that the examples of unrelated items do not correspond to the instant situation. This is not found persuasive because each Group requires structurally and functionally distinct gene sequences and encoded products, as stated in the last Office action. Given current resources, it is an undue burden on the PTO to search more than one type of sequence.

The requirement is still deemed proper and is therefore made FINAL.

The groups set forth in the restriction requirement have been modified slightly. Claim 109 will be examined to the extent that it reads on the elected Group I, namely a method using a single gene encoding a completely lethal toxin which does not need to be further modified or activated. Furthermore, the indication in the restriction requirement that claims 118-119 belonged to Group I was in error. Given the recitation in these claims of an operator and a repressor binding to the operator, these claims should have been placed in Group IV. The errors are regretted.

Claims 98-99, 101, 103-106 and 109-113 are examined in the Office action that follows.

Applicants urge that the substitute pages of the specification submitted with the preliminary amendment of 21 March 2001 should be entered, since they were entered in the PCT. The Examiner maintains that the instant application is not a national phase of a PCT application under 35 USC 371, but is instead a continuation of a PCT, with a separate U.S. specification. Thus, the rules for entry of amendments to the specification under 37 CFR 1.121(c) apply, and

any amendments made to the PCT specification during its prosecution are not automatically made in the instant continuation application.

The application is objected to because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c). A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required. See for example page 65.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 98-99, 101, 103-106 and 109-113 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of using a multitude of repressor gene sequences encoding a multitude of different products such as antisense RNA, ribozymes, or proteins encoded by sense sequences, each of a different sequence and from any source. In contrast, the specification only provides guidance for a sense repressor gene encoding a protein. No guidance is provided for the identification, isolation or characterization of a multitude of sequences encoding a multitude of antisense RNAs or a multitude of ribozymes of any sequence, corresponding to any gene of any sequence.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California* v. *Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus as broadly claimed. Given the lack of written description of the claimed products, any method of using them would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the claimed invention at the time of filing. See Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111).

Claims 98-99, 101, 103-106 and 109-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a method using a sense repressor gene encoding a protein, does not reasonably provide enablement for claims

broadly drawn to a method for using any repressor gene of any sequence encoding any type of product including antisense RNA or ribozymes for the repression of a lethal gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of using a multitude of repressor gene sequences encoding a multitude of different products such as antisense RNA, ribozymes, or proteins encoded by sense sequences, each of a different sequence and from any source. In contrast, the specification only provides guidance for a sense repressor gene encoding a protein. No guidance is provided for the identification, isolation or characterization of a multitude of sequences encoding a multitude of antisense RNAs or a multitude of ribozymes of any sequence, corresponding to any gene of any sequence. Furthermore, no guidance is presented for the evaluation or obtention of actual repression of lethal gene activity following the use of a multitude of non-exemplified antisense RNA-encoding or ribozyme-encoding sequences.

Antisense RNA-mediated gene inhibition is unpredictable. See Colliver et al, page 509, Abstract, who teach that antisense RNA actually *increased* rather than inhibited gene expression in some cases.

Furthermore, non-exemplified means of gene inhibition such as ribozymes have not been demonstrated to effect gene inhibition or phenotypic change *in planta*. See Evans et al, page 344S, paragraph bridging columns 1 and 2, who teach that neither cleavage of target RNA nor

reduction in the target gene product were observed in plant cells. See also Mazzolini et al, who teach low activity of ribozymes in intact plant cells and negligible reduction of enzyme activity following cell transfection with genes encoding ribozymes specific for the target enzyme, even when the ribozyme genes themselves were highly expressed (see, e.g., page 716, column 1, first full paragraph; page 722, bottom paragraph of each column; page 723, column 1; page 726, bottom paragraph of each column; page 728, column 2, first full paragraph; page 729, first full paragraph of column 1, first paragraph of column 2).

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify and isolate a multitude of non-exemplified antisense RNA-encoding or ribozyme-encoding sequences corresponding to a multitude of non-exemplified lethal genes, and to evaluate and obtain successful inhibition of lethal gene activity following plant transformation therewith.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 98-99, 103 and 109-113 are rejected under 35 U.S.C. 102(b) as being anticipated by Mariani et al (U.S. 5,689,041).

The claims are broadly drawn to a method of obtaining a plant which has a repressible lethal gene encoding a lethal product and a sense repressor gene encoding a protein which negates the activity of the lethal gene, wherein the lethal gene may be linked to a gene encoding a trait of interest, wherein the lethal and repressor genes are not linked, wherein at least one of the genes is under the control of a tissue-specific promoter, wherein individual plants each containing one of the genes may be crossed, and wherein at least one plant obtained from the progeny of the cross is homozygous for the genes.

Mariani et al teach plant transformation with a gene encoding resistance to stress, diseases, insects or herbicides linked to a lethal gene comprising a barnase (ribonuclease)-encoding sequence under the control of a tapetum-specific promoter, and plant transformation with a sense repressor gene comprising a barstar (ribonuclease inhibitor)-encoding sequence, wherein haploid plants may be transformed to produce homozygous plants following chromosome doubling or wherein plants homozygous for the transgene(s) may be obtained following selfing prior to outcrossing (see, e.g., column 14, lines 22-30; column 15, line 8 through column 19, line 38; claims 24-77). Given the random nature of plant transformation, the transgenes would inherently be integrated independently of each other, and any progeny could be evaluated for said independence merely by calculating genetic ratios of the progeny exhibiting particular trait.

Claims 98-99, 103-104 and 109-113 are rejected under 35 U.S.C. 102(e) as being anticipated by Mariani et al (U.S. 5,723,763 effectively filed March 1994).

The claims are broadly drawn to a method of obtaining a plant which has a repressible lethal gene encoding a lethal product and a sense repressor gene encoding a protein which negates the activity of the lethal gene, wherein the lethal gene may be linked to a gene encoding a trait of interest, wherein the lethal and repressor genes are not linked, wherein at least one of the genes is under the control of a tissue-specific promoter including a seed-specific promoter, wherein individual plants each containing one of the genes may be crossed, and wherein at least one plant obtained from the progeny of the cross is homozygous for the genes.

Mariani et al teach plant transformation with a gene encoding resistance to stress, diseases, insects or herbicides linked to a lethal gene comprising a barnase (ribonuclease)-encoding sequence under the control of a tapetum-specific promoter or a female reproductive tissue-specific promter including an ovule (seed)-specific promoter, and plant transformation with a sense repressor gene comprising a barstar (ribonuclease inhibitor)-encoding sequence, wherein haploid plants may be transformed to produce homozygous plants following chromosome doubling or wherein plants homozygous for the transgene(s) may be obtained following selfing prior to outcrossing (see, e.g., column 14, lines 7-14 and 59-67; column 15 through column 19, line 20; column 23, lines 40-55; claims 25-78). Given the random nature of plant transformation, the transgenes would inherently be integrated independently of each other, and any progeny could

be evaluated for said independence merely by calculating genetic ratios of the progeny exhibiting particular trait.

Claims 98-99, 103-104, 106 and 109-113 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/44465 (MONSANTO).

The claims are broadly drawn to a method of obtaining a plant which has a repressible lethal gene encoding a lethal product and a sense repressor gene encoding a protein which negates the activity of the lethal gene, wherein the lethal gene may be linked to a gene encoding a trait of interest, wherein the lethal and repressor genes are not linked, wherein at least one of the genes is under the control of a tissue-specific promoter including a seed-specific promoter, wherein individual plants each containing one of the genes may be crossed, and wherein the repressor gene may be under the control of an inducible promoter.

MONSANTO teaches plant transformation with an herbicide resistance gene linked to a seedling lethality gene comprising a seed-specific isocitrate lyase promoter or chemically inducible GmHSP26(GH2/4) promoter ligated to a sequence encoding antisense RNA to acyl CoA oxidase, and plant transformation with a sense gene encoding a yeast acyl CoA oxidase, wherein the antisense gene caused seedling lethality and the sense gene repressed the lethal effects, and also teaches crossing plants containing each gene wherein plants homozygous for each gene may also be obtained (see, e.g., page 15, lines 4-9; pages 23-32; claims 1, 3-9, 11-19, 21-29, 31-37). Given the random nature of plant transformation, the transgenes would inherently be integrated

independently of each other, and any progeny could be evaluated for said independence merely by calculating genetic ratios of the progeny exhibiting particular trait.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 98-99, 101, 103, 106 and 109-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al (U.S. 5,689,041).

The claims are broadly drawn to plant transformation with a lethal gene and repressor gene, wherein the two genes may be integrated on opposite sister chromosomes of a chromosome pair, and wherein a chemically inducible promoter may be used.

The teachings of Mariani et al have been discussed above. Mariani et al also teach the use of inducible promoters for their marker genes (see, e.g., column 12, lines 20-31 and claim 19, where wound- or light-inducible promoters are discussed).

Mariani et al do not explicitly teach the use of chemically inducible promoters or the identification of gene integration in opposite sister chromosomes.

It would have been obvious to one of ordinary skill in the art to utilize the method of controlling lethal gene expression taught by Mariani et al, and to modify that method by incorporating a chemically inducible promoter, given the advantages of inducible promoters for controlled heterologous gene expression as taught by Mariani et al, and the recognition by those of ordinary skill in the art that choice of known inducible promoter would have been the optimization of process parameters. Some of the progeny of the crosses would inherently contain gene integrations on sister chromosomes, given the random nature of plant transformation.

Claims 98-99, 101, 103-106 and 109-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al (U.S. 5,723,763 effectively filed March 1994).

The claims are broadly drawn to plant transformation with a lethal gene and repressor gene, wherein the seed-specific phaseolin promoter may be used, wherein the two genes may be integrated on opposite sister chromosomes of a chromosome pair, and wherein a chemically inducible promoter may be used.

The teachings of Mariani et al have been discussed above. Mariani et al also teach the use of inducible promoters for their marker genes (see, e.g., column 12, lines 7-17 and claims 42, 57 and 71, where wound- or light-inducible promoters are discussed).

Mariani et al do not explicitly teach the use of chemically inducible promoters or the identification of gene integration in opposite sister chromosomes, or the use of the phaseolin promoter.

It would have been obvious to one of ordinary skill in the art to utilize the method of controlling lethal gene expression taught by Mariani et al, and to modify that method by incorporating a chemically inducible promoter, given the advantages of inducible promoters for controlled heterologous gene expression as taught by Mariani et al, and the recognition by those of ordinary skill in the art that choice of known inducible promoter would have been the optimization of process parameters. Furthermore, given the teaching of Mariani et al to utilize an ovule (seed)- specific promoter, it would have been an obvious design choice to select any known seed-specific promoter such as the phaseolin promoter. Some of the progeny of the crosses would inherently contain gene integrations on sister chromosomes, given the random nature of plant transformation.

Claims 98-99, 101, 103-106 and 109-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/44465 (MONSANTO).

The claims are broadly drawn to plant transformation with a lethal gene and repressor gene, wherein the seed-specific phaseolin promoter may be used, and wherein the two genes may be integrated on opposite sister chromosomes of a chromosome pair.

The teachings of MONSANTO have been discussed above. MONSANTO do not teach the use of the phaseolin promoter or the integration of the genes on opposite chromosomes.

It would have been obvious to one of ordinary skill in the art to utilize the method for seed-specific lethal gene expression and repression taught by MONSANTO, and to modify that method by incorporating known seed-specific promoters such as the phaseolin promoter, given the recognition that choice of seed-specific promoter is an obvious design choice. Some of the progeny of the crosses would inherently contain gene integrations on sister chromosomes, given the random nature of plant transformation.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

January 13, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638